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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,864	12/20/2001	Thomas Ried	14014.0319U2	8947

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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,864	RIED ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,14-23 and 26* is/are pending in the application.

4a) Of the above claim(s) *21-23 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, and 14-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 12/23/2003 is acknowledged. Claims 1, 14, 15, 16, 17, 18, 19, and 20 are amended. Claim 26 is new.

Election/Restrictions

Claims 21-23, directed to an invention that is independent or distinct from the invention originally claimed for the reason of record. Accordingly, claims 21-23 are withdrawn from consideration as being directed to a non-elected invention for reason of record. See 37 CFR 1.142(b) and MPEP § 821.03.

New claim 26 is directed to a different invention because it has a different objective, and different effects. The examined invention is drawn to method of "screening presence of cancer cells" but the newly presented method is drawn to method of "substantially simultaneously visualizing epithelial origin of a cell". Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 26 is also withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

This application contains claims 21-23, and 26 drawn to an nonelected invention. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1, 14, 15, 16, 17, 18, 19, 20, 21-23, and 26 are pending. Claims 1, 14, 15, 16, 17, 18, 19, and 20 are under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

This Office action contains new grounds of rejection.

Claim Rejections - 35 USC § 102, Withdrawn

The rejection of claims under 35 U.S.C. 102(b) as being anticipated by WO 96/02002 (a copy provided with ISR, and IDS A4) is withdrawn because WO 96/02002 does not teach the new limitation "blood" and "circulating" epithelial cells.

Claim Rejections - 35 USC § 103, Maintained

Claims 1, 14, 15, 17, and 19 remain rejected for reason of record under 35 U.S.C. 103(a) as being unpatentable over either US Pat. 6,365,362 B1 (filing date Feb. 12, 1999) or Racila et al (IDS A26, cited in the previous Office action) for enriching step, and WO 97/38313 (IDS, and also cited in previous Office action) for detection step.

Claims 1, 14, 15, 17, and 19 are interpreted as drawn to method of detecting circulating cancerous epithelial cells by enriching said epithelial cells by cytokeratin screening, followed by detection of cancer cells using genetic marker specific probes capable of distinguishing cancerous cells from normal cells.

Applicant does not dispute that either US Pat. 6,365,362 B1 or Racila et al teach how to enrich circulating epithelial steps using cytokeratin screening or magnetic particles connected to a ligand capable of binding epithelial cells. Applicant argues that "[t]he circulating epithelial cells were simply assumed to be tumor cells" in Racilia et al (1998) and then says that "Jonathan Uhr is an author and contributor of Racila et al (1998) as well as an inventor of the present application." However, Jonathan Uhr is an

author and contributor of Racila et al (1998) as well as an inventor of the present application does not affect the teaching of Racila et al (1998) i.e. "Epithelial cells from patients with breast cancer generally stained with mABs against cytokeratin and 3 of 5 for mucin-1. In contrast, no cells that stained for these antigens were observed in the blood from normal controls. The morphology of the stained cells was consistent with that of neoplastic cells.": This statement in the abstract at least suggests that the epithelial cells are cancerous.

Applicant argues that WO97/38313 does not teach the instantly claimed enriching steps. This argument has been fully considered but found not persuasive because if the enriching steps of WO97/38313 were same as those of the instant claims, then the Office would have used WO97/38313 as 102 reference. Since WO97/38313 does not teach the same enriching step, WO97/38313 used as 103 reference along with US Pat. 6,365,362 B1 or Racila et al, that teaches the instantly claimed enriching step. As stated before in the previous Office action, WO97/38313 teaches all the reagents necessary to distinguish cancer cells from non-cancer cells using the hybridization pattern of nucleic acids (see page 21 to the first paragraph of page 26, especially page 22 line 2-8) and multiple probes (Example 7). The disclosed examples of probe associated with cancer and genetic markers are PSMA, PSA, and centromeric regions of chromosomes 7, 8, 18 (page 21-22). Further, WO97/38313 teaches methods of determining status and progress of cancer patient, and monitoring efficacy of cancer treatment at page 3 lines 18-26, page 25, lines 19-26, examples 2, 7 and 11. Also note claims 1, 6, 7, and 15-17, 26, 29, and 31. WO97/38313 teach

chromosomal aneuploidy is a strong indication of a cancerous state (see 1st para, page 22), thus WO97/38313 teaches the detection part of the instant claims.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to combine the teachings of US Pat. 6,365,362 B1 or Racila et al and WO97/38313 to use in method of detecting cancer cells in circulating blood because either Racila et al and 6,365,362 B1 suggests that enriching circulating epithelial cells using the method disclosed in Racila et al and 6,365,362 B1 is more sensitive than the method of WO97/38313. Therefore, one having ordinary skill in the art at the time the claimed invention would have been motivated to replace the enriching steps of WO97/38313 with the enriching steps of 6,365,362 B1 or Racila et al to arrive at more sensitive method with reasonable expectation of success since US Pat. 6,365,362 B1 or Racila et al teaches immunomagnetic enrichment is much more sensitive.

The Following Are New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 (in step b) recites "a probe under conditions capable of forming a complex with an antigen of the cell wherein the probe is associated with a specific

marker, thereby identifying the organ-origin of the cancer cell and wherein the probe is specific for a genetic marker", but it is not clear what the metes and bounds are. First it is not clear whether "a probe under conditions capable of forming a complex with an antigen of the cell" is the same as "the probe is specific for a genetic marker" and "the probe is associated with a specific marker". If they are not same, then the two "the probe" in the claim 20 (step b) lack antecedent basis. Second, it is not clear whether the detection step involves hybridization and immunocytochemistry simultaneously. The specification at page 26 under the heading "Diagnostic Application using Genetic Probes" teaches "genetic" is associated with nucleic acid material such as primers. The specification at page 25, first line teaches that "antigen" is a protein. Therefore the above limitation appears to say one probe is specific for "protein" and "nucleic acid".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection has two parts.

First, this is new matter rejection. Claim 20 (in step b) recites "a probe under conditions capable of forming a complex with an antigen of the cell wherein the probe is

associated with a specific marker, thereby identifying the organ-origin of the cancer cell and wherein the probe is specific for a genetic marker". This rejection is made because the Office interprets the two "the probe" recited in step b are same as "a probe" capable of detecting an antigen i.e. "protein". Applicant is kindly requested to point out the support for the limitation in the specification as originally filed since the support is not apparent to the Office.

Second, this is written description rejection. The limitation "a probe under conditions capable of forming a complex with an antigen of the cell wherein the probe is associated with a specific marker, thereby identifying the organ-origin of the cancer cell and wherein the probe is specific for a genetic marker" is interpreted as a probe capable of detecting a cancer antigen and also capable of hybridizing to a specific genetic material such that the hybridization pattern could tell where the cancer cells originated from.

The applicable standard for the written description requirement can be found in MPEP 2163, University of California v. Eli Lilly, 43 USPQ2d 1398 at 1407, and PTO Written Description Guidelines, Enzo Biochem Inc. v. Gen-Prove Inc., 63 USPQ2d 1609. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

The specification as originally filed teaches antibody capable of binding to an antigen of cell and also teaches probes capable of hybridizing to a genetic marker. The specification does not describe a single species of probe capable of forming a complex with an antigen of the cell and specific for a genetic marker.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of nucleic acid molecules, given that the specification has only described antibody binds to antigen and primers bind to genetic markers.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 16, 18, and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by 6,365,362 B1 (filing date Feb. 12,1999).

Claims 16 is drawn to method of determining status of cancer by determining amount of cancer cells in blood sample from a patient diagnosed with cancer using a probe capable of detecting an antigen of the cell. Claim 18 is drawn to method determining progress of cancer comprising the same steps as those of claim 16 above except that samples are collected in two (first and second) different points. Claim 20 is interpreted as drawn to method of determining effectiveness of cancer treatment using the same method of claim 16. The limitation "a probe under conditions capable of forming a complex with an antigen of the cell wherein the probe is associated with a specific marker, thereby identifying the organ-origin of the cancer cell and wherein the probe is specific for a genetic marker" is interpreted as drawn to contacting with a probe i.e. antibody.

6,365,362 B1 teaches method of determining status of cancer, determining progress of cancer, and determining effectiveness of cancer treatment by enumerating cancer cells by detecting complex formation between a probe and antigen of cells from a blood sample obtained from a patient diagnosed with cancer or administered anti-cancer therapy using a probe capable of detecting an antigen of the cell and also teaches obtaining samples twice for determining status or progression. Note Examples 3-8 at columns 26-31, abstract, claims 1-15, and Figs 1-8.

Thus, 6,365,362 B1 anticipates claims 16 and 18, 20.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne C Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1642

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